U.S.C.§101 on the basis that the claims were drawn to non-statutory subject matter.

Claims 1, 4-8 and 10 have been cancelled and new claims 21-27 have been drafted to avoid the rejection based on non-statutory subject matter. New claim 21 points out a product that contains non-human beta casein which does not contain the sequences SEQ ID 1 and 2. This language clearly defines a product that is not found in nature and is free of the rejection based on non-statutory subject matter. For this reason, it is requested that this ground of rejection be withdrawn.

Claims 1-11 and 16-20 were rejected under 35 U.S.C.§112, first paragraph as containing subject matter which was not described in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected to make and/or use the invention.

Reconsideration is requested.

It is established that non-human beta casein causes an immune response in humans. Cavallo demonstrated that lymphocytes from diabetic patients respond to bovine beta casein while patients affected by another autoimmune disease, such as ATD, do not respond to bovine beta-casein. This is persuasive evidence of the specificity of the immune response to bovine beta casein in patients with IDDM.

The evidence in support of the role of beta casein in the pathogenesis of IDDM comes from epidemiological date, animal experiments and studies on the immune response to bovine beta casein in IDDM patients. During the past fifteen years, several epidemiological studies, including time-series, ecological and case control studies have provided strong evidence for the role of bovine milk proteins in the pathogenesis of IDDM.

In 1984, a paper reported on the incidence of

IDDM in parts of Norway and Sweden and its association with a change in breast feeding frequency. It was found that there was a peak in the incidence of IDDM about 9 years after the time when breast feeding was at the lowest point. A strong association between cow's milk consumption and the incidence of IDDM in children (correlation coefficient=0.96) has been demonstrated using data from 12 countries world-wide. This relationship has been confirmed even within a single population by correlating fluid cow milk consumption and the incidence rates of IDDM in children in nine regions of Italy (correlation coefficient=0.84). Copies of the supporting papers will be provided to the Examiner upon request.

Experiments in NOD mice have demonstrated the influence of bovine milk proteins on the natural history of diabetes. In fact "it has been shown that a protein free diet in non-obese diabetic (NOD) mice, prevents the development of the disease while a diet containing casein as the only source of protein produces diabetes in the same animal model"(Cavallo, page 926, lines 2-6).

At page 927, col. 2, Cavallo proves that a proliferative response to beta casein in IDDM pat patient is a strong indication that such beta casein in involved in the onset of IDDM.

The claims are drawn to the prevention of IDDM in all patients since all individuals at birth can be potentially at risk and therefore all of theses individuals should not be exposed to an environmental risk factor such as cow's milk in their early life as clearly highlighted by the epidemiological studies cited above.

The applicant traverses the Examiner's assertion that the predicability in the art is extremely low because the available data points to a predictability of at least 50%. Cavallo is misleading in that the

percentages are derived from a generic population of individuals without any data regarding the percentage that was breast fed. In addition, the percentage referring to a healthy population is misleading in that subjects who do not show an immune response to bovine beta casein can still be considered candidates for the present invention since they may be exposed to bovine beta casein diet s at a later date after which they could develop IDDM.

The following facts support the enabling nature of the present application:

1. A decrease in breast feeding corresponds to an increase of IDDM which is a clear indication that exposing healthy subjects to bovine beta casein at a very early stage of life predisposes to IDDM on set.
2. There has been found a correspondence between sequences of beta casein (63-68) and residues 415-419 of the beta cell-specific glucose transporter GLUT 2.
3. There has been found proliferation of T-cells in the presence of beta casein and corresponding recognition of GLUT2, such T-cells only being present in IDDM patients.

The conclusion is straight forward: to prevent the onset of IDDM, the best thing to do is to feed all infants and new born with milk or dietary products free of the immunogenic peptides according to the present invention.

The experimentation that may be required to verify the above mentioned conclusion does not require undue experimentation as that term is used in the patent law. Tests to verify that the new diet reduces the incidence of IDDM are not difficult although they may require an extended time period. The experiment to establish that bovine beta casein induces autoimmunity to GLUT2 as well as T-lymphocytes in vitro to the same proteins can be easily measured by ELISA methods or by T-cell stimulation index tests.

The existence of an autoimmune response mechanism is well established. After Cavallo, a number of publications have confirmed the finding that t-cell lymphocytes proliferation response to bovine beta casein and antibodies to bovine beta casein occur in patients with IDDM. Moreover, it has been found that lymphocytes of diabetic patients recognize bovine beta casein as well as GLUT2 sequence in addition the epidemiological studies give a strong indication that to a decrease in breast feeding corresponds to an increase in the onset of IDDM. For these reasons, the present application provides an enabling disclosure as required by the first paragraph of 35 U.S.C.§112.

Claims 5, 6, 8, 16, 19 and 20 were rejected under 35 U.S.C.§112 for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

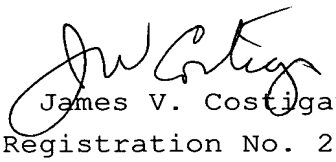
These claims have been cancelled and new claims have been added that are free of the formal grounds of rejection that were raised against the cancelled claims. For these reasons, it is requested that the newly presented claims be favorably considered.

The rejection of claims 1-6, 8, 10, 11, 16, 19 and 20 has been rendered moot by the cancellation of these claims. The newly presented claims refer to a product lacking specific sequences that are not disclosed by Bergstrom. The teachings of Bergstrom are essentially to obtain a milk from a non-human transgenic animal in which the beta casein obtained is human. The claims define a beta casein which is a non-human beta casein. For these reasons, it is requested that the Bergstrom reference not be used to reject the newly presented claims.

The Chianese reference and the Mukerji references do not disclose or suggest a beta casein which lacks the specific sequences that are recited in the newly present claims. The Le Magnen reference doses not disclose anything other than a casein removal process. It fails to suggest the specifically claimed beta casein which is recited in the newly presented claims. For these reasons, it is requested that these references not be applied to reject the newly presented claims.

An early and favorable action is earnestly solicited.

Respectfully submitted,



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